

## REMARKS

This amendment is submitted together with Applicants' Request for Continued Examination.

Applicants have amended claims 19 through 23, 27, 30, 34, 37 and 43 through 49, and added new claims 53 through 54. Antecedent basis for new claims 53 and 54 and for the amendments to claims 19 through 23, 27, 30, 34, 37 and 43 through 49 may be found in the specification on pages 6 through 8, and on page 15, lines 16 through 25. Claims 53 and 54 have been added to cover vectors comprising an isolated nucleic acid sequence from modified vaccinia Ankara virus where a heterologous sequence has been inserted either into an ECOR1 restriction site of or into an open reading frame of the ATI region of the isolated nucleic acid sequence for integration of a heterologous sequence into an ECOR1 restriction site of or into an open reading frame of the ATI region of an orthopoxvirus. Applicants have added these additional vector claims because vector claims 23 through 36 last presented have been amended to require the insertion of multiple cloning sites into an open reading frame of the ECOR1 site of the isolated nucleic acid sequence. Thus new independent claims were required to cover the vectors with the insertion of the heterologous sequence. Accordingly claims 19 through 54 are now in this application and are presented for examination.

Applicants wish to thank Examiner Mosher for granting their undersigned attorney a telephone interview held on

1 June 2006. A copy of the Examiner's Interview Summary Record is attached to this amendment. Examiner Mosher indicated that she wanted to change the language in all of the independent claims to delete "includes at least one restriction enzyme recognition site for a heterologous sequence and that...". The Examiner considers the language to be deleted as indefinite.

Applicants suggested, and Examiner Mosher then indicated that she agreed that including a statement in the independent claims that the respective nucleic acid sequence or the isolated fragment of the nucleic acid sequence capable of integration of a heterologous sequence through homologous recombination into an open reading frame or an ECORI site of the ATI region of an orthopoxvirus would be a positive step toward distinguishing the presently claimed invention over the cited prior art references including the MEYER et al, PAOLETTI et al, SHIDA et al, ANTOINE et al, ALTENBURGER et al and SUTTER et al references. However, the Examiner made it clear that in her opinion, inclusion of this limitation will still not be enough to distinguish the claims over the cited prior art, without some additional amendments. The Examiner insisted that all claims directed to the isolated nucleic acid sequence, the fragment of an isolated nucleic acid sequence, or vectors containing either the isolated nucleic acid sequence or the fragment of an isolated nucleic acid sequence, must include in addition, either an actual heterologous sequence inserted within an open reading frame or an ECORI site in the ATI region of the isolated nucleic acid sequence or isolated fragment of the nucleic

acid sequence from the modified vaccinia Ankara virus, or include in the isolated nucleic acid sequence or isolated fragment of the nucleic acid sequence, multiple cloning sites inserted into an open reading frame or an ECORI site thereof.

In the present amendment, Applicants have amended independent claims 19 and 21 to require in the isolated nucleic acid sequence or isolated fragment of the nucleic acid sequence, from the ATI region of modified vaccinia Ankara virus, multiple cloning sites inserted into an open reading frame or an ECORI site thereof. Applicants have also made the analogous amendments to independent vector claims 23 and 30. Vector claims 23 and 30 require that multiple cloning sites are inserted into an open reading frame or an ECORI site of either the isolated nucleic acid sequence or the isolated fragment of a nucleic acid sequence from modified vaccinia Ankara virus.

During the interview Examiner Mosher than suggested that Applicants include two additional independent claims to the vectors that do not require that multiple cloning sites are inserted into an open reading frame or an ECORI site of either the isolated nucleic acid sequence or the isolated fragment of a nucleic acid sequence from modified vaccinia Ankara virus. Thus Applicants have included new independent claims 53 and 54 that require an actual heterologous sequence inserted within an open reading frame or an ECORI site in the ATI region of the isolated nucleic acid sequence or isolated fragment of the nucleic acid sequence within the vector. Once again there is no suggestion in the prior art of

record to include within an open reading frame or within the ECORI site of the ATI region of an isolated nucleic acid sequence from modified vaccinia Ankara virus, a heterologous sequence.

The Examiner seems to be particularly concerned about the combination of SHIDA et al or PAOLETTI et al in combination with ANTOINE et al and ALTENBURGER as a basis for the obviousness of the claimed invention. Applicants pointed out to the Examiner that the MEYER et al reference discloses the instability of the ATI region of modified vaccinia Ankara virus (MVA) and that this region would be the last place where one "skilled in the art" would expect to integrate heterologous DNA to form a stable recombinant poxvirus. The Undersigned also emphasized that PAOLETTI et al does not disclose any integration of heterologous DNA sequences into the ATI region of a poxvirus, but instead discloses removal of the unstable ATI sequences and replacement of those sequences with more stable sequences. Only then is the heterologous sequence inserted. Furthermore the poxviruses specifically disclosed in PAOLETTI et al do not include MVA. Regarding SHIDA et al Applicants also emphasized that there is no specific disclosure of preparing recombinant MVA poxviruses, though other poxviruses are mentioned. Furthermore there is no actual disclosure in SHIDA et al of insertion of heterologous DNA into the ATI region of a poxvirus.

Applicants pointed out that all of the claims now require that the heterologous sequences or the multiple cloning sites be inserted into an open reading frame or an ECORI site of the ATI region of the isolated nucleic acid sequence or the

isolated fragment of the nucleic acid sequence and there is no such requirement disclosed or suggested in the cited prior art. Furthermore the claims to the recombinant poxviruses and the methods of preparing same require that a heterologous sequence be inserted into an open reading frame or an ECORI site of the ATI, and that there is no disclosure or suggestion of same in the prior art.

Applicants emphasize that according to the present application on page 7, central paragraph, the destruction of open reading frames, lying within the ATI region, by insertion of sequences, does not hamper the viral life cycle or replication efficiency and does not interfere with viral propagation or replication efficiency, respectively, of the recombinant poxviruses prepared according to the present invention. As also described by MEYER et al, sequence rearrangement occurred during cell culture propagation (see page 1036, right-hand column, lines 2 to 4, and the second paragraph of said column). Thus as a result of sequence deletions or frame-shift mutations within the ATI region, sequence rearrangements also occurred within said region. Accordingly such rearrangements created new open reading frames and that these open reading frames are important for replication and genome stability of the virus. It is therefore expected that the disruption of the open reading frames by integration of foreign sequences would seriously compromise the viral life cycle. For these reasons it can indeed be considered as surprising that this is not the case

when including sequences into an open reading frame of the ATI region of a poxvirus genome.

The Examiner agreed that the commonly assigned SUTTER et al references do not disclose or suggest insertion of the heterologous DNA into an open reading frame or an ECORI site of an isolated nucleic acid sequence or an isolated fragment of a nucleic acid sequence from the ATI region of MVA. The Examiner agreed that the deletion site II mentioned in SUTTER et al as the point of insertion of heterologous DNA is not the deletion site which includes the ATI region, which the Examiner indicates from MEYER et al is deletion site IV; see page 4, central paragraph, of the office action. Examiner Mosher was convinced that the invention as now presently claimed is patentably distinguishable from the SUTTER et al reference since the wrong deletion site for MVA is specifically disclosed in the reference.

Examiner Mosher also indicated that there will be no need to submit a terminal disclaimer to disclaim the terminal portion of any patent that may issue in this application beyond the expiration date of US Patent 6,440,422 to SUTTER et al since this reference does not suggest preparing a recombinant MVA by insertion of heterologous DNA into an open reading frame or the ECORI site of the ATI region of the MVA through homologous recombination.

Applicants believe that all claims now presented are in condition for allowance and a response to that effect is earnestly solicited. Applicants are enclosing PTO Form 2038 for

authorization to charge the filing fee for the Request for Continued Examination that accompanies this amendment to the charge account of the undersigned attorneys.

Respectfully submitted,  
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Enclosures: Examiner's Interview Summary Record  
PTO 2038 - 2 extra ind. claims



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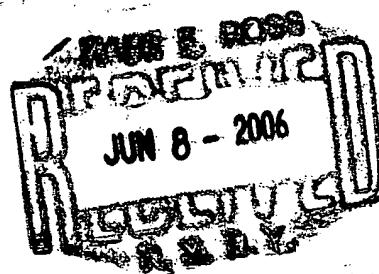
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MOSHER, MARY	
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Please find below and/or attached an Office communication concerning this application or proceeding.



<b>Interview Summary</b>	Application No. 10/668,521	Applicant(s) WINTERSPERGER ET AL.
	Examiner Mary E. Mosher, Ph.D.	Art Unit 1648

All participants (applicant, applicant's representative, PTO personnel):

(1) Mary E. Mosher, Ph.D.

(3) \_\_\_\_\_

(2) Jonathan myers.

(4) \_\_\_\_\_

Date of Interview: 01 June 2006.



Type: a)  Telephonic b)  Video Conference  
c)  Personal [copy given to: 1)  applicant 2)  applicant's representative]

Exhibit shown or demonstration conducted: d)  Yes e)  No.

If Yes, brief description: fax of amendment proposed by JM.

Claim(s) discussed: all pending.

Identification of prior art discussed: all cited in last action.

Agreement with respect to the claims f)  was reached. g)  was not reached. h)  N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: See Continuation Sheet.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

*Mary Mosher*  
MARY E. MOSHER, PH.D.  
PRIMARY EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required